

## **REMARKS**

The applicants acknowledge the Office Action of June 1, 2009, with appreciation. The Office indicates that Claims 22-56 are pending in the application, of those, Claims 22-37 and 54-56 are withdrawn from consideration. Claims 38-53 are presently under examination. The Applicant respectfully requests the Office acknowledgement of the status of pending Claims 57 and 58.

To begin, the Office acknowledges the Applicant's election of restriction group II, Claims 38-53, with traverse. The restriction requirement was traversed on the basis that the cited art do not teach the common linking feature unifying the inventions of Restriction Groups I-V. The Office was not persuaded. The Office concludes that the cited Hutchens describes sorbents having at least two different groups. The Office has made the restriction requirement Final.

### **GENERAL NOTE TO THE EXAMINER:**

With the instant response, the Applicant amends generic Claim 38 to include limitations (a)-(c). Support for the amendment may be found throughout the instant specification. In particular, support for limitation (b) may be found in the instant specification at page 33, lines 19-22. Support for limitation (c) may be found in the instant specification at page 50, lines 15-19. Furthermore, generic Claim 38 is amended to recite the limitations of Claim 41. Claim 41 is now redundant on the generic claim and is hereby canceled. Claim 42 is also canceled.

Moreover, the Applicant amends Claims 43, 44, 46, 49, 50, 51 and 52 to recite proper antecedent basis on the amended claims.

New Claim 59 is added to the Listing of Claims. Support for Claim 59 may be found in the instant specification at page 51, lines 5-8.

### **ANTICIPATION UNDER 35 USC § 102(b):**

Moving on, the Office rejects Claims 38-53 as being anticipated under 35 U.S.C. § 102(b) over the disclosure of Hutchens (WO 98/59360) in view of Hsich, et al., (U.S. Patent No. 6,176,268). The Office concludes that Hutchens discloses a method of retentate chromatography for resolving analytes in a sample. The Office cites Hsich, et al. for teaching that the Gibbs free energy contribution of binding events between the retained analyte and the sorbent are negative, indicating a favorable binding event that occurs without the addition of energy, as instantly claimed.

Claim 38 is presently amended to recite that the sorbent comprises a carrier and at least two different groups capable of binding. Support for the amendment may be found in the instant specification, for example, at page 8, lines 9-10. Moreover, generic Claim 38 is amended to recite that the at least two different groups capable of binding at step (ii) are inserted into a polymer via at least two identical or different functional groups of the polymer, whereby a polymer is formed which is derivatized with said groups, and further that said derivatized polymer is bound to the carrier by means of non-covalent interactions.

The instant invention relates to a method of selectively, at least bivalent binding, of a substrate as defined in Claim 38, which results in an improved separation selectivity of a substrate with respect to at least one substance to be separated off. Thus, a substrate is separated off from a mixture with at least one further accompanying substrate whereby the substrate, having at least two different groups capable of binding, forms a stronger bond with the at least two different groups of the sorbent than the accompanying substrate.

In the claimed at least bivalent binding, the absolute value of the determined Gibbs energies for the at least bivalent binding is greater than the sum of the absolute values of the Gibbs energies for the individual bonds of the groups. Only then a binding strengthening occurs that results in the improved separation selectivity.

The Applicant submits that Hutchens does not disclose a binding strengthening which results in improved separation selectivity. Moreover, the Applicant submits that Hsich, et al. do not teach such a binding strengthening.

The Office cites Hsich, et al. as teaching that Hutchens inherently discloses a negative value of the Gibbs energy. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). Hsich, et al. teach that to provide a favorable specific interaction between two dissimilar polymers leading to a negative contribution of the Gibbs free energy, one or both of the polymers must be modified to improve adhesion or miscibility. See Hsich, et al. at Column 8, lines 11-16.

The Applicant submits that the Office identification of disclosure of a negative value of Gibbs energy where one or more dissimilar polymers must be modified to improve adhesion or miscibility, does not support the Office conclusion that a negative value of Gibbs energy is inherent in the binding reactions described in Hutchens. Thus, Hsich, et al. do not support the Office conclusion that the Gibbs free energy contribution of binding events is inherent in the disclosure of Hutchens.

Further distinguishing the instant invention, generic Claim 38 manditorily requires the presence of two different groups capable of binding (the substrate), which are inserted into a polymer via at least two identical or different groups to form a derivatized polymer, as recited in part (b) of instant Claim 38, wherein the derivatized polymer is non-covalently bound to a carrier, as recited in part (c) of instant Claim 38.

The Applicant submits that Hutchens discloses a method of retentate chromatography for resolving "analytes". Hutchens uses a material comprising a substrate on which adsorbents are applied. Hutchens discloses polymers comprising adsorbents, for example, at page 7, line 13-25 as cited by the Office.

The Applicant notes that the passage does not disclose that at least two different groups capable of binding (adsorbents) are inserted into the polymer via at least two

identical or different groups to form a derivatized polymer, as in part (b) of the instant generic claim, nor that the derivatized polymer is non-covalently bound to a carrier (substrate), as in part (c) of instant Claim 38.

Furthermore, Hutchens discloses polymers comprising adsorbents in the section entitled "Substrate preparation" at page 26. Embodiments of producing the substrate are disclosed.

In one embodiment, the adsorbents can be bound to cross-linked polymers, which in turn, may be bound to the surface of the probe via a functional group. Mixtures of polymers may also be used, see page 28, lines 12-16.

Hutchens does not disclose that at least two different groups capable of binding (adsorbents) are inserted into the polymer via at least two identical or different groups to form a derivatized polymer, as in part (b) of instant Claim 38, nor does Hutchens disclose that the derivatized polymer is non-covalently bound to a carrier (substrate), as in part (c) of instant Claim 38.

Moreover, in a second embodiment, Hutchens discloses, at page 28, lines 17-20, that the adsorbent is bound to a first substrate which subsequently is positioned onto a second substrate. The adsorbents can be bound to polymeric beads (line 23).

The Hutchens reference does not disclose that at least two different groups capable of binding (adsorbents) are inserted into the polymer via at least two identical or different groups to form a derivatized polymer, as in part (b) of instant Claim 38, nor does Hutchens disclose that the derivatized polymer is non-covalently bound to a carrier (substrate), as in part (c) of instant Claim 38.

Hutchens discloses another embodiment wherein the adsorbent may be bound directly to the substrate by covalent or non-covalent binding, see page 29, lines 7-9. The substrate may be an organic polymer (see page 27, line 12).

Thus, Hutchens does not disclose that at least two different groups capable of binding (adsorbents) are inserted into the polymer via at least two identical or different groups to form a derivatized polymer, as in part (b) of instant Claim 38, nor does Hutchens disclose that the derivatized polymer is non-covalently bound to a carrier (substrate), as in part (c) of instant Claim 38.

Hutchens discloses an embodiment at page 29, lines 10-20, wherein the adsorbent may be fixed directly onto the substrate, wherein the adsorbent itself is polymer. However, Hutchens neither discloses that at least two different groups capable of binding (adsorbents) are inserted into the polymer via at least two identical or different groups to form a derivatized polymer, as in part (b) of instant Claim 38, nor that the derivatized polymer is non-covalently bound to a carrier (substrate), as in part (c) of instant Claim 38.

Hutchens discusses polymers at page 30, lines 19-30 and page 31, line 1-10. The disclosure in Hutchens refers to the synthesis of different polymeric adsorbents. The polymeric adsorbents are synthesized by attaching a precursor molecule to the substrate, initiating the polymerization reaction, and terminating the polymerization reaction at varied degrees of completion for each adsorbent. Significantly, Hutchens neither discloses that at least two different groups capable of binding (adsorbents) are inserted into the polymer via at least two identical or different groups to form a derivatized polymer, as in part (b) of instant Claim 38, nor that the derivatized polymer is non-covalently bound to a carrier (substrate), as in part (c) of instant Claim 38.

Furthermore, Hutchens discusses adsorbents having a mixed functionality at page 44, line 12. However, this passage neither discloses that at least two different groups capable of binding (adsorbents) are inserted into the polymer via at least two identical or different groups to form a derivatized polymer, as in part (b) of instant Claim 38, nor that the derivatized polymer is non-covalently bound to a carrier (substrate), as in part (c) of instant Claim 38.

The Applicant submits that Hutchens does not disclose each and every element as set forth in the claims, and therefore, Hutchens does not anticipate the instantly claimed invention.

Moreover, the Applicant submits that Hutchens does not disclose the instantly claimed, "at least bivalent binding" and binding strengthening as in part (a) of generic Claim 38.

Hutchens discloses adsorbent arrays at page 89 and page 90 which are used for the solution of a specific separation problem. The adsorbent arrays are produced by adding adsorbents (1) to (5), or alternatively, adsorbents (1) to (6) to various spots. The disclosure is restricted to the statement that a silicon oxide coated stainless steel substrate is coated with each adsorbent (1) to (5). Moreover, the disclosure is restricted to the statement that various spots of a carbonized PEEK polymer substrate is coated with different adsorbents (1) to (6). Each adsorbent (1) to (5) defined at page 89, or (1) to (6), defined at page 90, has only one binding function. Hutchens explicitly discloses that one adsorbent, having only one binding function, is added to one spot.

According to Hutchens, at page 28, line 3, such a probe spot has a diameter of approximately 3 mm. Due to this spacial arrangement, the adsorbent arrays of Hutchens may not be capable of forming an "at least bivalent binding", since for the formation thereof, based on the dimensions of the molecules to be bound, the binding sites must have distances from each other that are in the molecular range, not in the millimeter range as disclosed. Therefore, Hutchens does not disclose an "at least bivalent binding", let alone a binding strengthening, as instantly claimed.

Furthermore, with respect to the Office conclusion that Hutchens discloses a method characterized in that the adsorbent has at least two groups capable of binding, the Applicant submits that Hutchens discloses that the substrate is coated with an adsorbent. Hutchens disclose the addition of terminal functional groups,  $\text{-NH}_3$  group or  $\text{-COO}^-$ ; but not  $\text{-NH}_3$  group and  $\text{-COO}^-$ . Moreover, the binding properties of the arrangement vary in a one- or two-dimensional gradient. For example, the substrate

is provided in the form of a strip, which is at one end weakly hydrophobic and at the other end, strongly hydrophobic, or in the form of a plate, which is in one corner weakly hydrophobic and anionic in the other corner, see page 31, line 11-16 of Hutchens. Hutchens describes the arrangement to be "Incremental Gradient Adsorbent Surfaces" and discloses binding of a substance to sorbents by varying the binding affinity via a gradient, but not by an "at least bivalent binding" as instantly claimed. In the arrangements disclosed in Hutchens, it is submitted that at least bivalent binding cannot take place due to the spatial arrangement of the adsorbents. Consequently, Hutchens does not disclose at least bivalent binding, let alone a binding strengthening, as instantly claimed.

As noted by the Office, Hutchens discloses adsorbents having mixed functionality. These are adsorbents having two or more bases of attraction by means of which analytes having two or more different bases of attraction may be resolved, see for example page 44, lines 21-32. Although Hutchens teaches that the mixed functionality adsorbent may exhibit hydrophobic interactions and negatively charged ionic interactions so as to bind hydrophobic analytes which are positively charged, Hutchens does not disclose that the different binding interactions occur simultaneously (hydrophobic/hydrophobic and ionic/ionic), or independently from each other (hydrophobic/hydrophobic or ionic/ionic). In the latter case, the analyte which has failed to be bound by hydrophobic interaction would be bound by ionic interaction, and vice versa.

Thus, Hutchens is silent with respect to "at least bivalent binding", wherein a binding strengthening occurs, which results in an improved separation selectivity with respect to an at least one substance to be separated off, as instantly claimed.

Thus, the Applicant submits that Hutchens does not disclose every element as set forth in the claims, either expressly or inherently, and therefore, may not anticipate the instantly claimed invention. Reconsideration and withdrawal of the rejection for anticipation over the disclosure of Hutchens is respectfully requested.

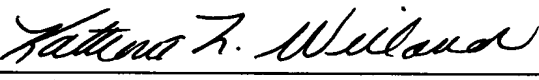
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Accordingly, entry of the present Response and Amendment into the record of this application and swift and favorable action on the merits thereof, are respectfully solicited.

It should be apparent that the undersigned has made an earnest effort to place this application into condition for immediate allowance. If she can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call the below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,  
THE FIRM OF HUESCHEN AND SAGE

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Enclosure: Listing of Claims; Extension of time fee under 37 CFR 1.17(a)(3) in the form of a check in the amount of \$555.00 (small entity) and Postal Card Receipt.

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**THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.**